



## REMARKS

As a result of the foregoing amendment, the claim has been amended to overcome the rejection under the second paragraph of 35 USC 112. Essentially the language suggested by the Examiner has been adopted. This rejection should be withdrawn.

Reconsideration and withdrawal of the rejection of new claim 2 as being unpatentable under 35 USC 103 (a) over MEDLINE AN 92210058 ('058) reference are respectfully requested.

The claim as presently presented now reads on a composition which contains a anti respiratory infectious disease preventing effective amount of compound (1). The reference contains no suggestion of any composition which contains this compound in a respiratory infectious disease preventing amount. Indeed, the reference does not disclose that this compound has such a property.

The reference discloses the effect of carbocysteine for the prevention or therapeutic treatment of inflammation of the bronchial mucosai as a result of the exposure to sulfur dioxide gas. The activity of the carbocysteine in the present invention differs from that of the reference with respect to the effective amount in that the target disease is different.

In particular, the reference relates to the development of inflammation due to SO<sub>2</sub> in the atmosphere. Such inflammation can develop only at the local area exposed directly to the SO<sub>2</sub> gas.

In contrast, the disease targeted by the present invention is an infective disease caused by bacteria and which occurs as a result of the multiplication of the bacteria attached to the surface of the upper respiratory tract. The infected area can expand broadly with the multiplication of such bacteria. As a result, the infected area develops to a systemic symptom which can complicate other various types of inflammation.

The reference only discloses that the carbocysteine disclosed therein is effective for the prevention of the inflammation due to the exposure of sulfur dioxide. The reference cites the activity of the carbocysteine and improving the visco-elastic properties of the bronchial muci *in vivo* and discloses that the effect is due to the increase of activity of sialyl transferase. In essence, the reference discloses that the inflammation is restrained by the protective effect of the bronchial mucosai membranes and enhanced by the physiological activity of the carbocysteine.

This contrasts completely with the effect and mechanism of the presently claimed composition. The carbocysteine component of the claimed composition prevents the attachment of the bacteria to the upper respiratory tract and thus excludes the source of the bacterial infection. Thus, this composition is a preventative and does not provide a systematic treatment for inflammation that has already been developed.

The inventor has studied the preventative effect of the presently claimed composition and has found that when an S-carboxymethylcysteine is used in the pharyngeal epithelial cell, the

number of bacteria adhering on the epithelial cells decreases. As bacteria with negative surface charges attached to the positively charged domain, i.e., microplicae of human pharyngeal epithelial cells, the inventor studies shows that the decrease of attachment of NTHI with epithelial cells after the treatment with S-CMC was due to the decrease of surface charges. Thus, the S-CMC decreases the episodes of respiratory infection in patients with respiratory diseases both by inhibiting the attachment o the bacteria to the upper respiratory tract and by detaching those that are adhered.

In the reference, the experiment which was conducted in the environment which was exposed to SO<sub>2</sub> gas on the assumption that the affection is caused by the SO<sub>2</sub> generated in the atmosphere by aerial pollution and the like. The pharyngeal epithelial cell were exposed continuously and chronically during the indicated period.

In contrast, the experiment with respect to bacterial infection in the present invention was conducted on the assumption of the subject encountering by accident the infectious bacterial and the exposure could be only to a small amount of bacteria. Obviously, once the bacteria get into the upper respiratory tract, they adhere and can multiply.

The reference simply does not contain any information which would lead one skilled in the art to conclude that one can have a respiratory infectious disease preventing effective amount of this compound or that it would indeed exhibit such properties. Consequently, the reference simply does not render the present invention as claimed obvious.

With respect to the Ogihara reference which the examiner indicated was not considered since an English translation was not provided, applicants will provide such a translation.

In view of the foregoing, it is submitted that this application is in condition for allowance and favorable reconsideration and prompt notice of allowance are earnestly solicited.

Respectfully submitted,

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